Advanced Regression: Bias and variance trade off and penalised splines

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Principles of non-linear regression

Concepts we cover in this lecture:

- The basics of cross validation
- Bias-variance trade-off in prediction
- Penalised splines

A clarification

> Note
>
> **Aim of prediction**: Define a prediction rule that is accurate, but also generalises to new data.

When performing prediction we split the data into the following three subsets:

- Training data to fit the models
- Validation data to estimate extra parameters of the prediction rule
- Test data to assess the generalisation properties

Training and test data

Assume we have the following data:

- Training data
  - y_i, where $i \in 1, ..., n$
  - x_i, vector of $j \in 1, ..., p$ predictors for observation k
- Test data
  - y_k^{Test}, where $k \in 1, ..., m$
  - x_k^{Test}, vector of $j \in 1, ..., p$ predictors for observation k
- We assume the following general model to hold for both training and test data

$$y = f(x) + \epsilon$$

Measuring the quality of fit

1. Based on the training data we build a prediction rule $\hat{f}(x)$

$$\hat{y}_i = \hat{f}(x_i)$$

For example the ordinary least squares prediction rule is defined as

$$\hat{y} = hy = x(x^t x)^{-1} x^t y = x\beta.$$

2. We evaluate the prediction rule $\hat{f}(x)$ (derived from the training data) on the test data x_k^{Test} and obtain the prediction $\hat{y}_k^{Test}$

$$\hat{y}_k^{Test} = \hat{f}(x_k^{Test}).$$

Mean squared error (MSE)

- It is easy to derive the MSE on the training data, this is equivalent to the residual sum of squares.
- The residual sum of squares do not tell us how well the prediction rule generalises to new data, the test data.

MSE evaluated on the test data

$$MSE = \frac{1}{m}\sum_{k=1}^{m}\left(\underbrace{y_k^{Test}}_{\text{Observed}} - \underbrace{\hat{f}(x_k^{Test})}_{\text{Predicted}}\right)^2$$

Decomposition into bias and variance

$$\begin{aligned} E(MSE) &= E(\frac{1}{m}\sum_{k=1}^{m}\left(y_k^{Test} - \hat{f}(x_k^{Test})\right)^2) \qquad (1)\\ &= \underbrace{\sigma^2}_{\text{Noise}} + \underbrace{E[\hat{f}(x_k^{Test}) - E(\hat{f}(x_k^{Test}))]^2}_{\text{Variance}} + \qquad (2)\\ &+ [E(\hat{f}(x_k^{Test})) - \hat{f}(x_k^{Test})^2] \qquad (3) \end{aligned}$$

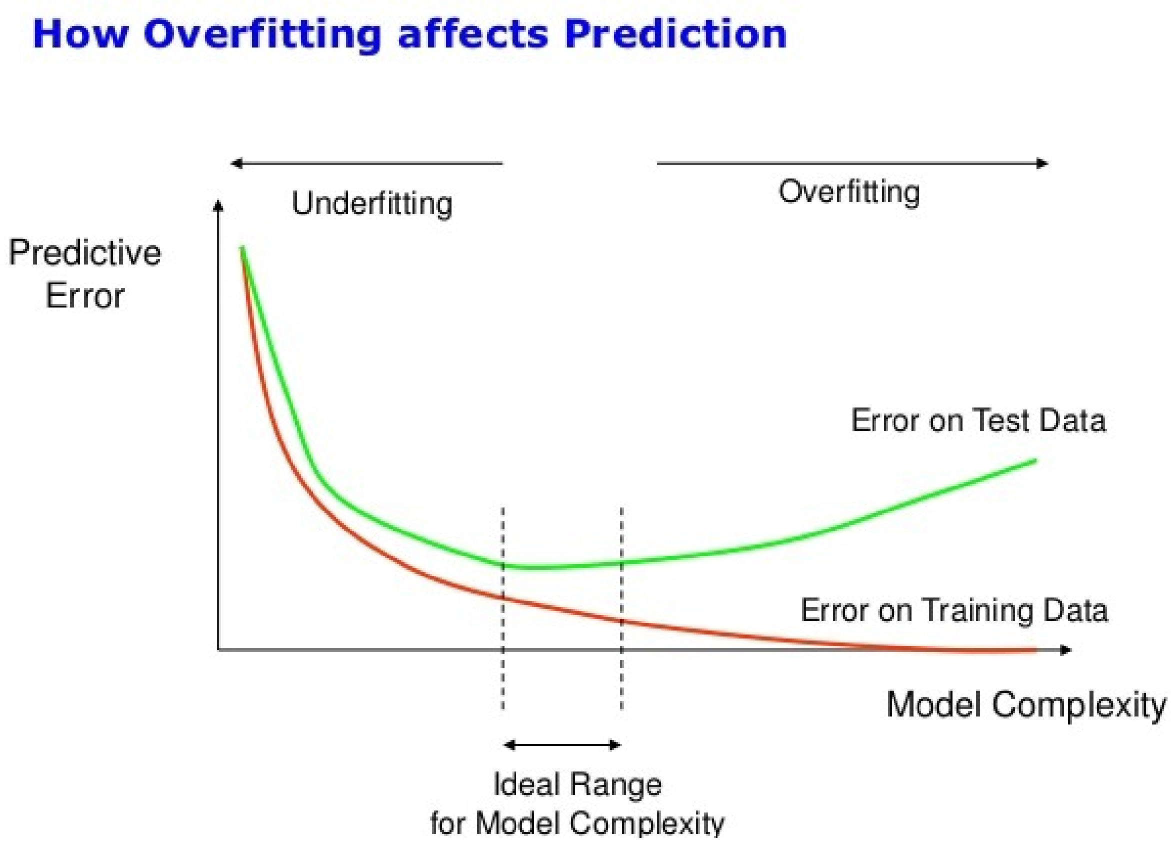
- Noise or irreducible error σ^2
- Variance $E[\hat{f}(x_k^{Test} - E(\hat{f}(x_k^{Test}))]^2$
- Bias $[E(\hat{f}(x_k^{Test})) - \hat{f}(x_k^{Test})]$

Bias-variance trade-off in prediction

- **Bias**: The error that is introduced by fitting the model.
  - More variables reduce the residual sum of squares.
  - We can reduce bias by adding more variables (higher complexity).
- **Variance**: The amount by which $\hat{f}(x)$ would change if we estimated it using a different training data set.
  - The more variables we include, the more likely $\hat{f}(x)$ will differ for a new training data
  - We can reduce variance by removing variables (lower complexity)

Overfitting

- Training MSE: We can always reduce the MSE by adding more variables (higher complexity).
- Test MSE: After the model is saturated, we will increase the MSE by adding more variables.



The problem of overfitting

Overfitting the data

- Complex models may be too precise and tailored only to the specific data used as training data.
- They follow the error or noise too closely.
- Complex models may provide perfect fit and very low MSE on the training data.

- But when used to build a prediction rule for new data they will have a high MSE on the test data.
- Thus, they do not generalise well to new data and do not provide a good prediction rule.

Measuring the quality of fit: Binary outcome

- Quantitative outcomes: Mean squared error (MSE)
- Binary outcome (Lecture 4):
  - Sensitivity and specificity
  - Misclassification error rate: Proportion of misclassified observations
  - Positive predictive value (PPV)

$$
\begin{aligned}
\text{PPV} + & \frac{\text{Number of true positives}}{\text{Number of true positives} + \text{Number of false positives}} && (4) \\
= & \frac{\text{Number of true positives}}{\text{Number of positive calls}} && (5)
\end{aligned}
$$

Bias-variance trade-off in estimation

- Consider an estimate $\hat{\theta}$ for a parameter θ.
- Examples:
  - Sample mean $\bar{x} = \frac{1}{n}\sum_{i=1}^{n} x_i$ for the population mean.
  - Sample variance $s^2 = \frac{1}{n-1}\sum_{i=1}^{n}(x_i - \bar{x})^2$ for the population variance.

Bias of an estimate

$Bias(\hat{\theta}) = E\left(\hat{\theta} - \theta\right)$

Bias-variance trade-off in estimation

Mean squared error (MSE) of an estimate $\hat{\theta}$:

MSE is the squared average difference between an estimate $\hat{\theta}$ and the true parameter θ.

$$
\begin{aligned}
MSE(\hat{\theta}) &= E(\hat{\theta} - \theta)^2 && (6)\\
&= (E(\hat{\theta}^2) - 2E(\hat{\theta})\theta + \theta^2) && (7)\\
&= (E(\hat{\theta}^2) - \underbrace{E(\hat{\theta})^2 + E(\hat{\theta})^2}_{0} - 2E(\hat{\theta})\theta + \theta^2) && (8)\\
&= (E(\hat{\theta}^2) - E(\hat{\theta})^2 + (E(\hat{\theta})^2 - 2E(\hat{\theta})\theta + \theta^2 && (9)\\
&= Var(\hat{\theta}) + (Bias(\hat{\theta}))^2 && (10)
\end{aligned}
$$

Bias-variance trade-off in estimation

Also in estimation there is a trade-off between bias and variance

$$MSE(\hat{\theta}) = Var(\hat{\theta}) + \left(Bias(\hat{\theta})\right)^2$$

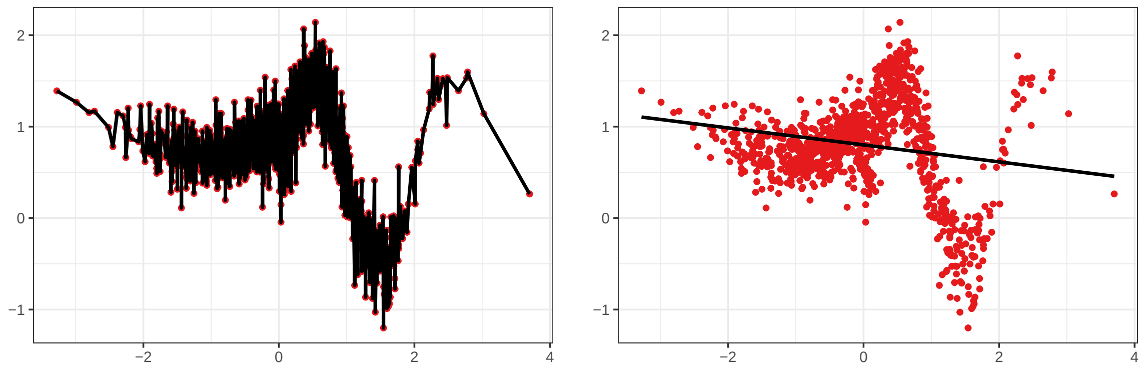
where

- $Var(\hat{\theta}) = E(\hat{\theta}^2) - E(\hat{\theta})^2$
- $Bias(\hat{\theta}) = E(\hat{\theta}) - \theta = E(\hat{\theta} - \theta)$

Many classical techniques are designed to be unbiased (BLUE) or consistent (Maximum Likelihood).

Recall previous problem

- Can you identify issues with bias and variance?
- How can we select the best fit?



Generic considerations

In regression splines, the smoothness of the fitted curve is determined by:

- the degree of the spline
- the specific parameterization
- the number of knots
- the location of knots

No general selection method for number and position of knots

Notice

The type of splines we have seen so far allow the use of standard estimation methods, derived by minimizing the usual least square objective:

$$\sum_i \left(Y_i - \beta_0 - f(x;\beta) + \sum_p \gamma_p z_p \right)^2,$$

where $f(x;\beta) = \sum_j \beta_j b_j(x_i)$ the splines basis function, z a set of other covariates with corresponding coefficients γ.

A penalised approach

A general framework of smoothing methods is offered by generalized additive models (GAMs).

GAMs extends traditional GLMs by allowing the linear predictor to depend linearly on unknown smooth functions. In the linear case:

$$Y_i = \beta_0 + f(x;\beta) + \sum_p \gamma_p z_p + \epsilon_i$$

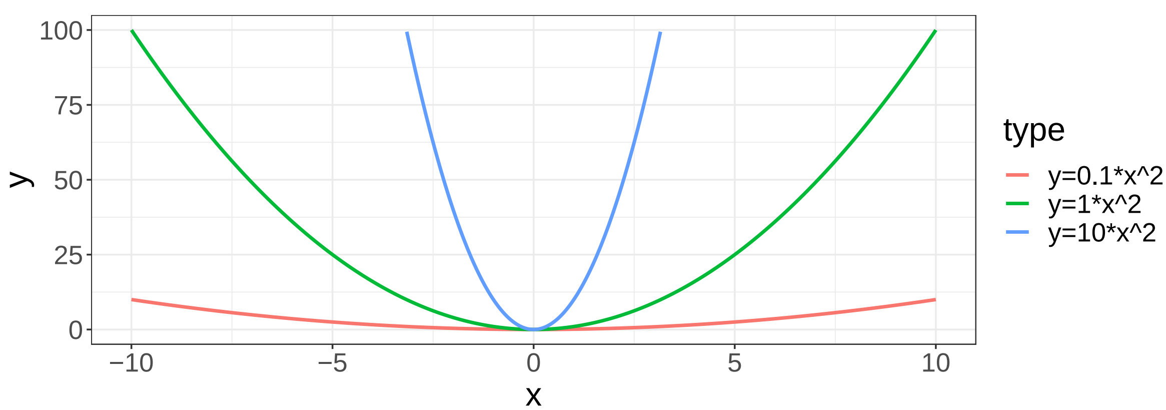
The idea is to define a flexible function and control the smoothness through a penalty term, usually on the second derivative.

Curvature

The second derivative of a function corresponds to the curvature or concavity of the graph. What do you observe?

```
Warning: Using `size` aesthetic for lines was deprecated in ggplot2 3.4.0.
i Please use `linewidth` instead.
```

```
Warning: Removed 684 rows containing missing values (`geom_line()`).
```



So if $f(x;\beta)$ is the spline basis function we defined, then we need to somehow introduce its second derivative $d^2f(x;\beta)/dx = f''(x;\beta)$ in the problem and 'scale' it so we have the 'best' fit.

Penalized splines

The objective now is to minimise the ‘augmented‘ sum of squares error:

$$\sum_i \left(Y_i - \beta_0 - f(x;\beta) + \sum_p \gamma_p z_p \right)^2 + \lambda \int [f''(x;\beta)]^2 dx$$

with λ being the smoothing parameter (variance-bias trade off).

Smoothers

Alternative smoothers available, differing by parameterization and penalty:

- Thin-plane splines
- Cubic splines
- P-splines
- Random effects
- Markov random fields
- kernels
- Soap film smooths
- …

Selecting smoothness

There are different ways of selecting/estimating λ

- The ordinary cross-validation (OCV) criterion, also known as the leave-one-out cross-validation (LOO-CV) criterion, seeks to find the λ that minimizes:

$$\text{OCV}(\lambda) = \frac{1}{n} \sum_i (Y_i - g_\lambda^{[i]}(x_i))^2$$

- The generalised cross-validation (GCV) criterion (an improvement of the OCV)
- AIC and BIC
- REML and ML

Example 1

A data frame giving a series of measurements of head acceleration in a simulated motorcycle accident, used to test crash helmets.

```r
library(MASS)
```

```

Attaching package: 'MASS'

The following object is masked from 'package:patchwork':

    area
```

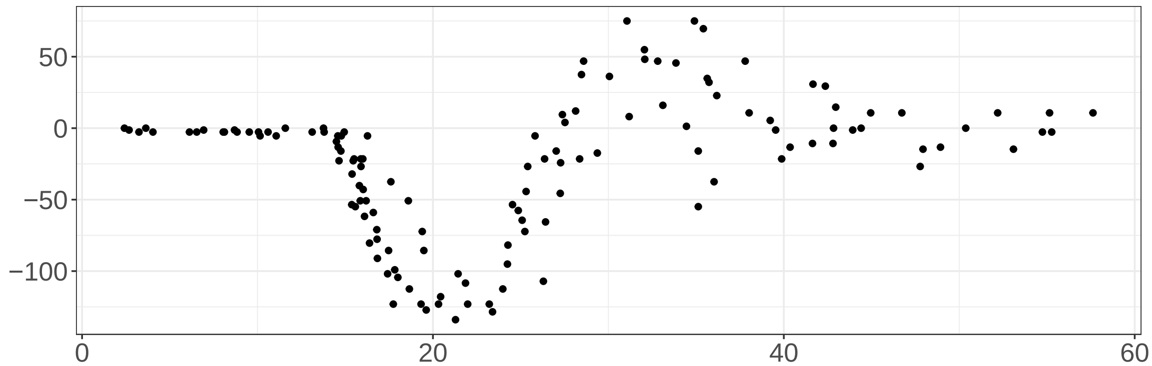
```r
library(dplyr)
```

```

Attaching package: 'dplyr'

The following object is masked from 'package:MASS':

    select

The following objects are masked from 'package:stats':

    filter, lag

The following objects are masked from 'package:base':

    intersect, setdiff, setequal, union
```

```r
data(mcycle)
mcycle %>% head()
```

```
  times accel
1   2.4   0.0
2   2.6  -1.3
3   3.2  -2.7
4   3.6   0.0
5   4.0  -2.7
6   6.2  -2.7
```

Example 1



Any ideas?

Example 1

I will use the pspline package to showcase how the selection of λ with GVC works:

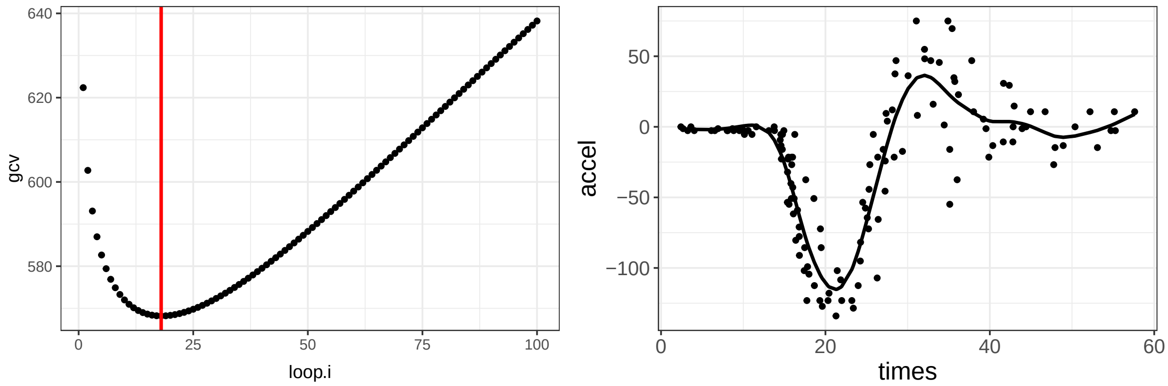
```
library(pspline)
```

```
Warning: package 'pspline' was built under R version 4.3.1
```

```
seq(from = 1, to = 100, length.out = 100) -> loop.i
gcv <- numeric(length(loop.i))

for (i in 1:length(loop.i)) {
  smooth.Pspline(mcycle$times, mcycle$accel,
    df = 4,
    spar = loop.i[i], method = 1
  ) -> mod.loop
  gcv[i] <- mod.loop$gcv
}

ggplot() +
  geom_point(aes(x = loop.i, y = gcv), cex = 1.3) +
  geom_vline(xintercept = loop.i[gcv %>% which.min()], col = "red", cex = 1) +
  theme_bw() -> p1
```

```r
smooth.Pspline(mcycle$times, mcycle$accel,
  df = 4, spar = loop.i[gcv %>% which.min()],
  method = 1
) -> mod.loop
ggplot() +
  geom_point(data = mcycle, aes(x = times, y = accel), cex = 1.3) +
  theme_bw() +
  geom_line(aes(x = mcycle$times, y = mod.loop$ysmth), cex = 1) -> p2
```

Example 1



Example 1 using GAM

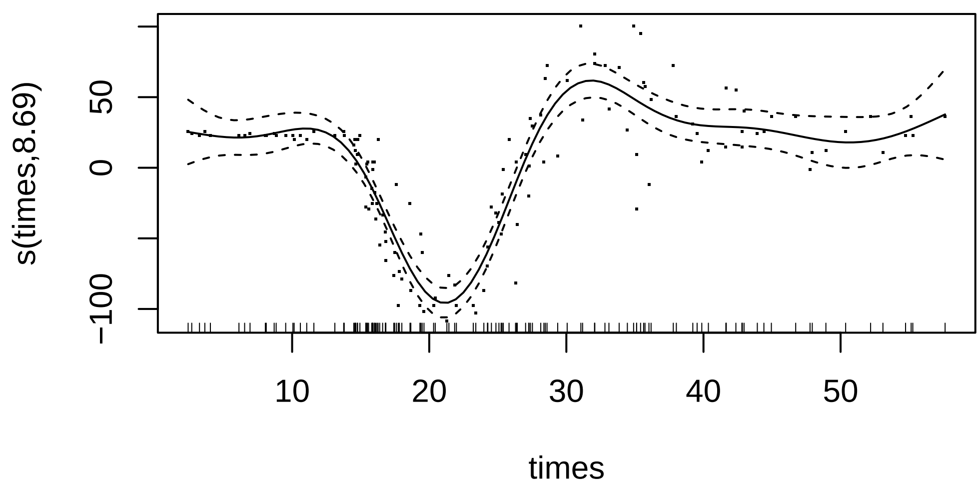
```r
mgcv::gam(accel ~ s(times), data = mcycle) -> mod.gam
mod.gam %>% summary()
```

```
Family: gaussian
Link function: identity

Formula:
accel ~ s(times)

Parametric coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  -25.546      1.956  -13.06   <2e-16 ***
```

```
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Approximate significance of smooth terms:
           edf Ref.df     F p-value    
s(times) 8.691  8.972 53.13  <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

R-sq.(adj) =  0.782   Deviance explained = 79.7%
GCV = 548.58  Scale est. = 508.61    n = 133
```

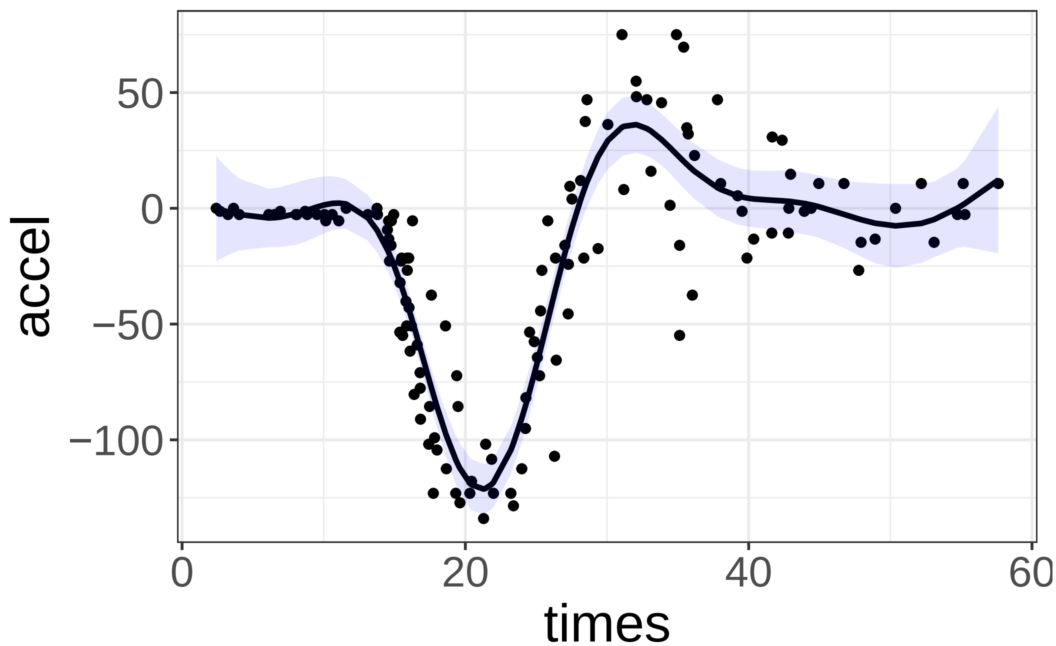
Example 1 using GAM

```
mod.gam %>% plot(se = TRUE, residuals = TRUE, cex = 0.5)
```



Example 1 using GAM

```
mgcv::gam(accel ~ s(times), data = mcycle) -> mod.gam
predict(mod.gam, data.frame(times = mcycle$times), se.fit = TRUE) -> preds

UL <- preds$fit + 1.96 * preds$se.fit
LL <- preds$fit - 1.96 * preds$se.fit

ggplot() +
  geom_point(data = mcycle, aes(x = times, y = accel), cex = 1.3) +
  theme_bw() +
  geom_line(aes(x = mcycle$times, y = preds$fit), lwd = 1) +
  geom_ribbon(aes(ymin = LL, ymax = UL, x = mcycle$times), fill = "blue", alpha = 0.1) +
  theme(text = element_text(size = 20))
```



Case-study: Chicago - Temperature and mortality

- Temperature is known to increase all-cause mortality rates
- In such studies, we need to carefully account for the temporal aspect (long-term trends and seasonality)

- We also need to properly account for factors that could confound the observed relationship.

GOAL: Use GAMs to explore the effect of temperature on mortality counts in Chicago.

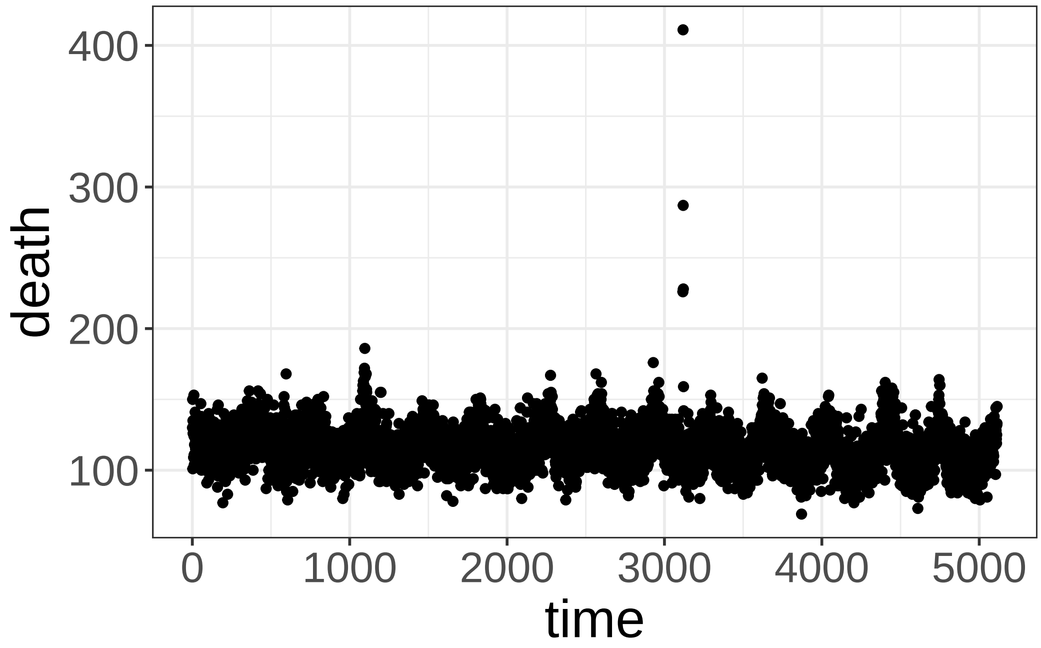
Case-study: Chicago - Temperature and mortality

```r
library(dlnm)

data(chicagoNMMAPS)
chicagoNMMAPS %>% head()
```

```
        date time year month doy      dow death cvd resp       temp   dptp
1 1987-01-01    1 1987     1   1 Thursday   130  65   13 -0.2777778 31.500
2 1987-01-02    2 1987     1   2   Friday   150  73   14  0.5555556 29.875
3 1987-01-03    3 1987     1   3 Saturday   101  43   11  0.5555556 27.375
4 1987-01-04    4 1987     1   4   Sunday   135  72    7 -1.6666667 28.625
5 1987-01-05    5 1987     1   5   Monday   126  64   12  0.0000000 28.875
6 1987-01-06    6 1987     1   6  Tuesday   130  63   12  4.4444444 35.125
    rhum     pm10       o3
1 95.500 26.95607 4.376079
2 88.250       NA 4.929803
3 89.500 32.83869 3.751079
4 84.500 39.95607 4.292746
5 74.500       NA 4.751079
6 77.375 40.95607 6.334412
```

Case-study: Chicago - Temperature and mortality

```r
ggplot() +
  geom_point(data = chicagoNMMAPS, aes(x = time, y = death), cex = 1.3) +
  theme_bw() +
  theme(text = element_text(size = 20))
```



Case-study: Chicago - Temperature and mortality

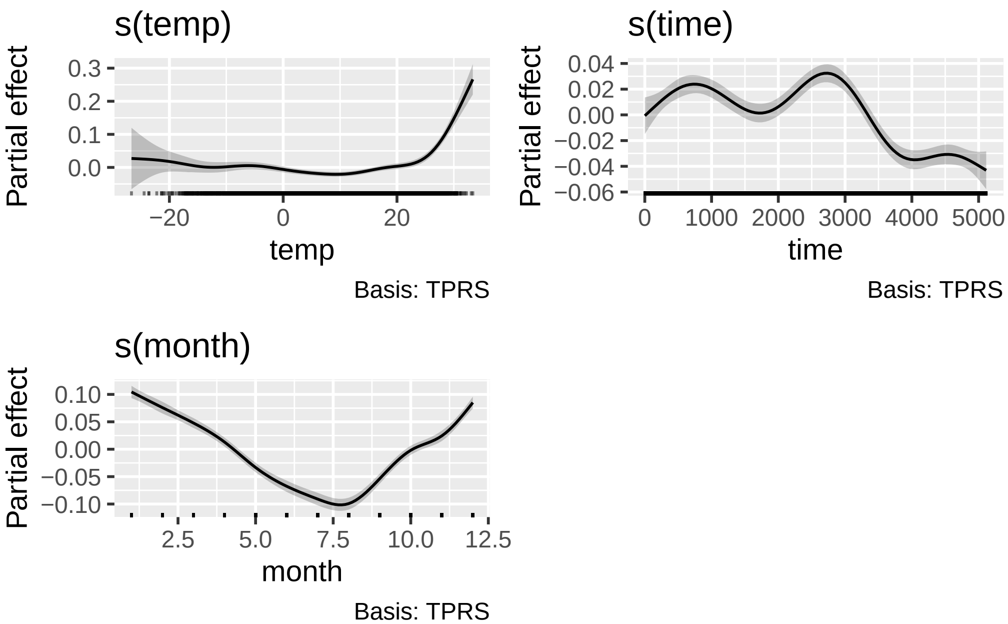
```
mgcv::gam(
  death ~ s(temp) +
    s(time) + s(month) + dow,
  data = chicagoNMMAPS, family = "poisson"
) -> res.mod

summary(res.mod)
```

```
Family: poisson
Link function: log

Formula:
death ~ s(temp) + s(time) + s(month) + dow

Parametric coefficients:
             Estimate Std. Error  z value Pr(>|z|)
(Intercept)  4.727980   0.003476 1360.069  < 2e-16 ***
dowMonday    0.034849   0.004874    7.150 8.71e-13 ***
```

```
dowTuesday   0.027304   0.004884    5.590 2.27e-08 ***
dowWednesday 0.010857   0.004904    2.214  0.02683 *
dowThursday  0.013197   0.004899    2.694  0.00707 **
dowFriday    0.019705   0.004891    4.029 5.61e-05 ***
dowSaturday  0.022413   0.004888    4.585 4.54e-06 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Approximate significance of smooth terms:
           edf Ref.df Chi.sq p-value
s(temp)  8.332  8.847  238.9  <2e-16 ***
s(time)  7.705  8.573  330.6  <2e-16 ***
s(month) 8.504  8.934  524.2  <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

R-sq.(adj) =  0.256   Deviance explained = 27.4%
UBRE = 0.41407  Scale est. = 1         n = 5114
```

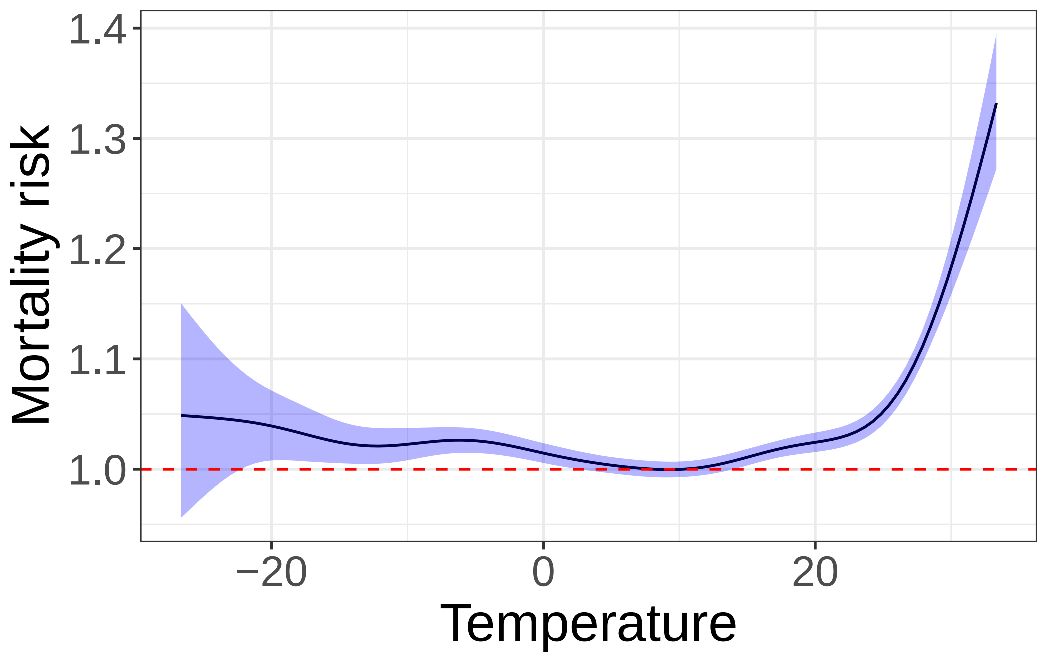
Case-study: Chicago - Temperature and mortality

```r
gratia::draw(res.mod)
```



Case-study: Chicago - Temperature and mortality

```r
gratia::smooth_estimates(res.mod) %>%
  gratia::add_confint() %>%
  filter(smooth == "s(temp)") %>%
  mutate(
    est = exp(est), lower_ci = exp(lower_ci), upper_ci = exp(upper_ci),
    temp = round(temp, digits = 2), rr = est / est[temp == 10.30],
    rr_upper = upper_ci / est[temp == 10.30],
    rr_lower = lower_ci / est[temp == 10.30]
  ) %>%
  ggplot() +
  geom_line(aes(temp, rr)) +
  geom_ribbon(aes(x = temp, ymin = rr_lower, ymax = rr_upper),
              alpha = 0.3, fill = "blue", col = NA) +
  geom_hline(yintercept = 1, col = "red", linetype = "dashed") +
  theme_bw() +
  ylab("Mortality risk") +
  xlab("Temperature") +
  theme(text = element_text(size = 20))
```



Case-study: Chicago - Temperature and mortality

How is the intercept interpreted? How the daily effect?

```
mgcv::gam(
  death ~ s(temp) +
    s(time) + s(month) + dow + s(pm10),
  data = chicagoNMMAPS, family = "poisson"
) -> res.mod1

res.mod1 %>% summary()
```

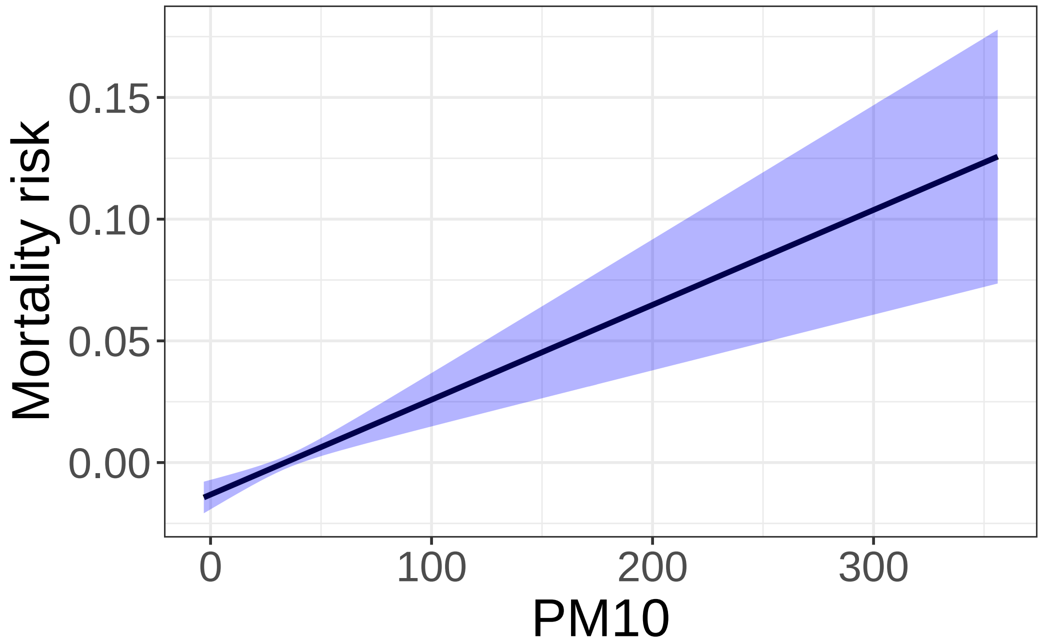
```
Family: poisson
Link function: log

Formula:
death ~ s(temp) + s(time) + s(month) + dow + s(pm10)

Parametric coefficients:
             Estimate Std. Error  z value Pr(>|z|)
```

```
(Intercept)  4.731117   0.003637 1300.968  < 2e-16 ***
dowMonday    0.030381   0.005079    5.982 2.21e-09 ***
dowTuesday   0.021400   0.005066    4.224 2.40e-05 ***
dowWednesday 0.007126   0.005095    1.399  0.16186
dowThursday  0.007744   0.005087    1.522  0.12792
dowFriday    0.015253   0.005094    2.994  0.00275 **
dowSaturday  0.019715   0.005043    3.909 9.25e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Approximate significance of smooth terms:
           edf Ref.df Chi.sq p-value
s(temp)  8.314  8.840  172.7 < 2e-16 ***
s(time)  7.817  8.639  310.0 < 2e-16 ***
s(month) 8.475  8.926  431.9 < 2e-16 ***
s(pm10)  1.001  1.002   22.5 1.8e-06 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

R-sq.(adj) =  0.256   Deviance explained = 27.5%
UBRE = 0.4123  Scale est. = 1         n = 4863
```

Case-study: Chicago - Temperature and mortality

Let's add the effect of air-pollution (PM10):

```r
gratia::smooth_estimates(res.mod1) %>%
  gratia::add_confint() %>%
  filter(smooth == "s(pm10)") %>%
  ggplot() +
  geom_line(aes(pm10, est), lwd = 1) +
  geom_ribbon(aes(x = pm10, ymin = lower_ci, ymax = upper_ci),
              alpha = 0.3, fill = "blue", col = NA) +
  theme_bw() +
  ylab("Mortality risk") +
  xlab("PM10") +
  theme(text = element_text(size = 20))
```



Case-study: Chicago - Temperature and mortality

```
res.mod1 %>% summary()
```

```
Family: poisson
Link function: log

Formula:
death ~ s(temp) + s(time) + s(month) + dow + s(pm10)

Parametric coefficients:
             Estimate Std. Error  z value Pr(>|z|)
(Intercept)  4.731117   0.003637 1300.968  < 2e-16 ***
dowMonday    0.030381   0.005079    5.982 2.21e-09 ***
dowTuesday   0.021400   0.005066    4.224 2.40e-05 ***
dowWednesday 0.007126   0.005095    1.399  0.16186
dowThursday  0.007744   0.005087    1.522  0.12792
dowFriday    0.015253   0.005094    2.994  0.00275 **
dowSaturday  0.019715   0.005043    3.909 9.25e-05 ***
---
```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Approximate significance of smooth terms:
           edf Ref.df Chi.sq p-value
s(temp)  8.314  8.840  172.7 < 2e-16 ***
s(time)  7.817  8.639  310.0 < 2e-16 ***
s(month) 8.475  8.926  431.9 < 2e-16 ***
s(pm10)  1.001  1.002   22.5 1.8e-06 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

R-sq.(adj) =  0.256   Deviance explained = 27.5%
UBRE = 0.4123  Scale est. = 1         n = 4863
```

Case-study: Chicago - Temperature and mortality

Lag effect

The effect of an exposure might not only affect the same day's health outcome, but also the health outcome in the subsequent days.

Lets explore the temperature lags independently in Chicago.

Case-study: Chicago - Temperature and mortality

```r
k <- c(0, 1, 3, 5, 10, 20)
res_store <- list()

for (i in 1:length(k)) {
  chicagoNMMAPS$temperature_laggeg <- lag(chicagoNMMAPS$temp, n = k[i])

  mgcv::gam(
    death ~ s(temperature_laggeg) +
      s(time) + s(month) + dow + pm10,
    data = chicagoNMMAPS, family = "poisson"
  ) %>%
    gratia::smooth_estimates() %>%
    gratia::add_confint() %>%
    filter(smooth == "s(temperature_laggeg)") %>%
    mutate(
      est = exp(est),
```

```r
      lower_ci = exp(lower_ci),
      upper_ci = exp(upper_ci),
      temperature_laggeg = round(temperature_laggeg, digits = 2),
      rr = est / est[temperature_laggeg == 10.30],
      rr_upper = upper_ci / est[temperature_laggeg == 10.30],
      rr_lower = lower_ci / est[temperature_laggeg == 10.30],
      lag = paste0("lag", k[i])
    ) -> res_store[[i]]
}


do.call(rbind, res_store) %>%
  mutate(lag = factor(lag, levels = c(paste0("lag", k)))) %>%
  ggplot() +
  geom_line(aes(temperature_laggeg, rr, col = lag), lwd = 1) +
  geom_ribbon(aes(x = temperature_laggeg, ymin = rr_lower,
                  ymax = rr_upper, fill = lag), alpha = 0.3, col = NA) +
  geom_hline(yintercept = 1, col = "red", linetype = "dashed", lwd = 1) +
  theme_bw() +
  ylab("Mortality risk") +
  xlab("Temperature") +
  ylim(c(0.7, 1.7)) +
  scale_fill_viridis_d(option = "C") +
  scale_color_viridis_d(option = "C") -> p28
```

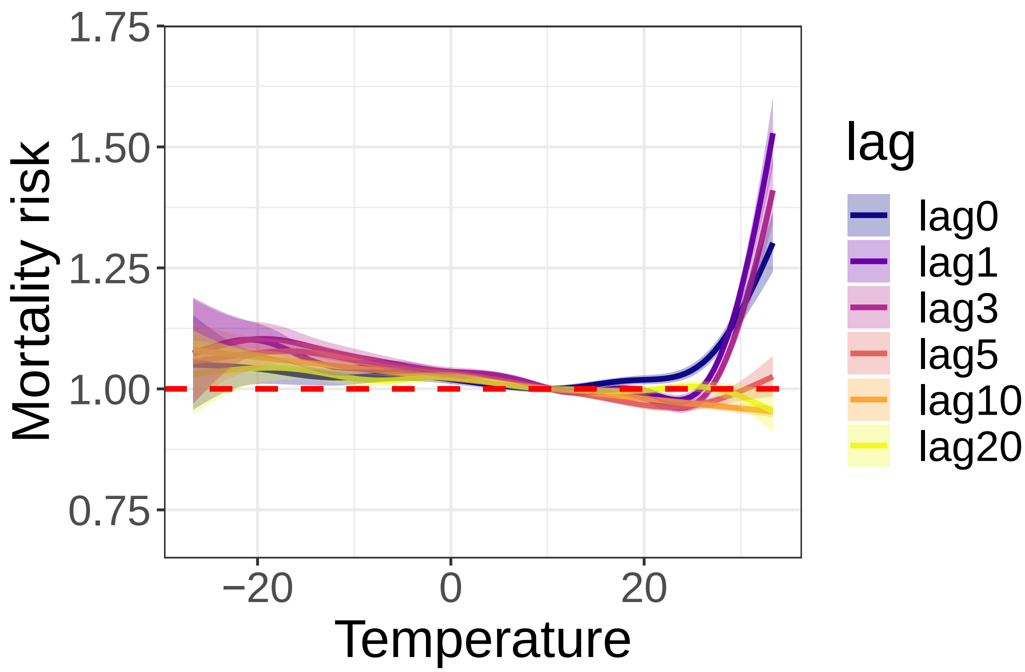
Case-study: Chicago - Temperature and mortality

- What do you observe?
- Why curves are similar?
- Is independence a valid assumption?

Summary

- Introduction to bias and variance trade off
- Theory and application of penalised splines
- How can we model lags properly?

Questions?


1.75
1.50
1.25
1.00
0.75
Mortality risk
−20
0
20
Temperature
lag
lag0
lag1
lag3
lag5
lag10
lag20